AMENDMENTS

In the claims:

Please cancel claims 7-11, 18, 21, and 79-80 (as indicated below) without prejudice to further prosecution in one or more related continuation or divisional applications. Please amend claims 1-6, 12-17, 19, 22-23, 26, 72-74, and 76-77, and add new claims 81-126 as follows:

1. (Currently Amended) A method of performing high throughput mass spectrometry screening, the method comprising:

(i) providing one or more cell comprising a gene library,

(~~i~~ ii) growing the one or more cell in vitro thereby providing non-column separated components comprising a library of gene expression products;

(~~ii~~ iii) purifying ~~a~~ samples comprising the non-column-separated components ~~containing one or more non-column-separated component from the one or more cell, the purifying comprising~~ with an off-line parallel purification system,

wherein the non-column-separated components have not undergone prior separation on a chromatography column;

(~~iii~~ iv) injecting the purified samples generated from step (iii) ~~sample containing one or more non-column-separated component~~ into a mass spectrometer~~, wherein the non-column-separated component has not undergone prior separation on a chromatography column~~; and~~,~~

(~~iv~~ v) performing flow-injection analysis using electrospray tandem mass spectrometry on the purified samples ~~the one or more non-column-separated component from the one or more cell~~ to detect the presence of one or more component of interest, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening of the one or more ~~non-column-separated component~~ component of interest,

wherein the one or more component of interest is from the one or more cell.

2. (Currently Amended) The method of claim 1, wherein step ~~(i)~~ (ii) occurs simultaneously with step ~~(ii)~~ (iii), and wherein said one or more cell is alive during step ~~(ii)~~ ~~(iii)~~.

3. (Currently Amended) The method of claims 1 or 2, wherein at least about 100 ~~cell colonies~~ samples are screened for presence of the one or more ~~non-column-separated~~ component of interest in less than an hour.

4. (Currently Amended) The method of claim 1, wherein at least about 200 ~~cell colonies~~ samples are screened for presence of the one or more ~~non-column-separated~~ component of interest in less than an hour.

5. (Currently Amended) The method of claim 1, wherein at least about 500 ~~cell colonies~~ non-column-separated samples are screened for presence of the one or more ~~non-column-separated~~ component of interest in less than an hour.

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6. (Currently Amended) The method of claim 1, wherein at least about 1000 ~~cell colonies~~ samples are screened for the presence of the one or more ~~non-column-separated~~ component of interest in about 1 day.

7-11. (Canceled)

12. (Currently Amended) The method of claim 1, wherein said purifying one or more non-column-separated ~~component~~ samples comprises performing step ~~(ii)~~ (iii) in a volatile buffer, a buffer that reduces concentration of ionic species, an ion exchange resin, or an organic solvent.

13. (Currently Amended) The method of claim 1, wherein the ~~non-column-separated components are produced from whole cells,~~ non-column-separated samples comprise cell lysate~~,~~ ~~cell supernatant or from reactions of purified cell enzymes with added substrates.~~

14. (Currently Amended) The method of claim 1, wherein the one or more ~~non-column-separated~~ component of interest is selected from~~:~~ the group consisting of a protein, a protein binding molecule, a carbohydrate, a carbohydrate binding molecule, a product of an enzyme catalyzed reaction, a nucleic acid, and a product of a nucleic acid catalyzed reaction.

15. (Currently Amended))The method of claim 1, wherein the one or more ~~non-column-separated~~ component of interest is selected from: an enzyme, an enzyme substrate, and an enzyme product.

16. (Currently Amended) The method of claim 1, wherein the ~~one or more non-column-separated~~ component of interest is selected from: a substrate with one or more hydrophobic moieties, an inorganic ion, an oligosaccharide, a hydrophobic molecule, atrazine, and a polyketide.

17. (Currently Amended) The method of claim 1, wherein purifying the ~~one or more~~ non-column-separated ~~component~~ samples comprises attaching the library of expression products ~~one or more non-column-separated components~~ to a solid support.

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18. (Cancel)

19. (Currently Amended) The method of claim ~~18~~ 17, wherein the ~~one or more non-separated column component~~ library of expression products comprises a library of enzymes, which enzymes each comprises a tag moiety, and wherein the solid support comprises a tag binding moiety.

20. (Original) The method of claim 19, wherein the tag moiety comprises biotin, avidin, or streptavidin and the tag binding moiety comprises biotin, avidin, or streptavidin.

21. (Canceled)

22. (Currently Amended) The method of claim ~~18~~ 1, wherein the one or more ~~non-column-separated component~~ component of interest ~~comprises~~ comprise ~~one or more~~ enzyme substrate and ~~one or more~~ product of an enzymatic reaction, the method further comprising simultaneously quantifying the amount of the ~~one or more~~ product of an enzyme reaction and the ~~one or more~~ enzyme substrate.

23. (Currently Amended) The method of claim ~~18~~ 1, wherein performing flow injection analysis using electrospray tandem mass spectrometry comprises performing a method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry.

24. (Original) The method of claim 23, comprising performing the neutral loss mass spectrometry or the parent ion mass spectrometry on a triple quadrupole mass spectrometer.

25. (Currently Amended) The method of claim 24, wherein performing the neutral loss mass spectrometry comprises:

(a) scanning the one or more ~~non-column-separated-component~~ component of interest in a first quadrupole at a specified mass range;

(b) fragmenting the one or more ~~non-column-separated-component~~ component of interest in a second quadrupole by collision induced dissociation, thereby producing one or more neutral fragments and one or more daughter ion; and,

(c) detecting the one or more daughter ion.

26. (Currently Amended) The method of claim 24, wherein performing the parent ion mass spectrometry comprises:

(a) scanning the one or more ~~non-column-separated-component~~ component of interest in a first quadrupole;

(b) fragmenting the one or more ~~non-column-separated-component~~ component of interest in a second quadrupole by collision induced dissociation; and,

(c) scanning a third quadrupole at a specified mass.

72. (Currently Amended) The method of claim 1, wherein purifying comprises centrifugation ~~of cells~~.

73. (Currently Amended) The method of claim 1, wherein purifying comprises filtration ~~of cells~~.

74. (Currently Amended) The method of claim ~~5~~ 1, wherein the off-line parallel purification system comprises an ion exchange resin.

75. (Previously Added) The method of claim 1, wherein the off-line parallel purification system comprises the addition of an organic solvent to the sample.

76. (Currently Amended) The method of claim 1, wherein the off-line parallel purification system comprises a solid phase extraction plate.

77. (Currently Amended) The method of claim 1, wherein an automatic sampler transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis at a rate of at least 100 samples ~~or more~~ an hour.

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78. (Previously Added) The method of claim 1, wherein 5 to 100 non-column separated samples are pooled before performing flow-injection analysis using electrospray tandem mass spectrometry.

79. (Canceled)

80. (Canceled)

81. (New) The method of claim 1, wherein the non-column separated samples comprise whole cells.

82. (New) A method of performing high throughput mass spectrometry screening, the method comprising:

(i) providing one or more cell comprising a gene library,

wherein the gene library encodes an enzyme library;

(ii) growing the one or more cell in vitro thereby providing non-column-separated components comprising an enzyme library;

(iii) purifying the samples comprising the non-column-separated components with an off-line parallel purification system,

wherein the purified non-column-separated components have not undergone prior separation on a chromatography column;

(iv) contacting the purified samples generated from step (iii) with an enzyme substrate to provide purified samples comprising a product of an enzymatic reaction;

(v) injecting the purified samples comprising the product of an enzymatic reaction into a mass spectrometer; and

(vi) performing flow-injection analysis using electrospray tandem mass spectrometry on the purified samples that comprise product of an enzymatic reaction, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening to detect the presence of one or more component of interest,

wherein the one or more component of interest is selected from the group consisting of the enzyme substrate, the product of an enzymatic reaction, and an enzyme.

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83. (New) The method of claim 82, wherein step (ii) occurs simultaneously with step (iii), and wherein said one or more cell is alive during step (iii).

84. (New) The method of claim 82, wherein at least about 100 samples are screened for presence of the one or more component of interest in less than an hour.

85. (New) The method of claim 82, wherein at least about 200 samples are screened for presence of the one or more component of interest in less than an hour.

86. (New) The method of claim 82, wherein at least about 500 samples are screened for presence of the one or more component of interest in less than an hour.

87. (New) The method of claim 82, wherein at least about 1000 samples are screened for the presence of the one or more component of interest in about 1 day.

88. (New) The method of claim 82, wherein the non-column-separated samples comprise cell lysate.

89. (New) The method of claim 82, wherein the non-column-separated samples comprise whole cells.

90. (New) The method of claim 82, wherein purifying the non-column-separated samples comprises attaching the enzyme library to a solid support.

91. (New) The method of claim 90, wherein each enzyme in the library further comprises a tag moiety, and wherein the solid support comprises a tag binding moiety.

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92. (New) The method of claim 91, wherein the tag moiety comprises biotin, avidin, or streptavidin and the tag binding moiety comprises biotin, avidin, or streptavidin.

93. (New) The method of claim 81, wherein the one or more component of interest comprises the enzyme substrate and the product of an enzymatic reaction, the method further comprising simultaneously quantifying the amount of the product of an enzyme reaction and the enzyme substrate.

94. (New) The method of claim 82, wherein performing flow injection analysis using electrospray tandem mass spectrometry comprises performing a method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry.

95. (New) The method of claim 94, comprising performing the neutral loss mass spectrometry or the parent ion mass spectrometry on a triple quadrupole mass spectrometer.

96. (New) The method of claim 95, wherein performing the neutral loss mass spectrometry comprises:

(a) scanning the one or more component of interest in a first quadrupole at a specified mass range;

(b) fragmenting the one or more component of interest in a second quadrupole by collision induced dissociation, thereby producing one or more neutral fragments and one or more daughter ion; and,

(c) detecting the one or more daughter ion.

97. (New) The method of claim 95, wherein performing the parent ion mass spectrometry comprises:

(a) scanning the one or more component of interest in a first quadrupole;

(b) fragmenting the one or more component of interest in a second quadrupole by collision induced dissociation; and,

(c) scanning a third quadrupole at a specified mass.

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98. (New) The method of claim 82, wherein purifying comprises centrifugation.

99. (New) The method of claim 82, wherein purifying comprises filtration.

100. (New) The method of claim 82, wherein the off-line parallel purification system comprises an ion exchange resin.

101. (New) The method of claim 82, wherein the off-line parallel purification system comprises the addition of an organic solvent to the sample.

102. (New) The method of claim 82, wherein the off-line parallel purification system comprises a solid phase extraction plate.

103. (New) The method of claim 82, wherein an automatic sampler transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis at a rate of at least 100 samples an hour.

104. (New) The method of claim 82, wherein 5 to 100 samples are pooled before performing flow-injection analysis using electrospray tandem mass spectrometry.

105. (New) A method of performing high throughput mass spectrometry screening, the method comprising:

(i) providing one or more cell comprising a gene library,

wherein the gene library encodes an enzyme library;

(ii) growing the one or more cell in vitro to provide an enzyme library;

(iii) contacting the enzyme library with an enzyme substrate thereby providing non-column-separated components comprising the enzyme library and product of an enzymatic reaction;

(iv) purifying samples comprising the non-column-separated components with an off-line parallel purification system,

wherein the non-column-separated components have not undergone prior separation on a chromatography column;

(v) injecting the purified samples into a mass spectrometer; and,

(vi) performing flow-injection analysis using electrospray tandem mass spectrometry on the purified samples, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening for presence of one or more component of interest,

wherein the component of interest is selected from the group consisting of the enzyme substrate, the product of an enzymatic reaction, and an enzyme.

106. (New) The method of claim 105, wherein at least about 100 samples are screened for presence of the one or more component of interest in less than an hour.

107. (New) The method of claim 105, wherein at least about 200 samples are screened for presence of the one or more component of interest in less than an hour.

108. (New) The method of claim 105, wherein at least about 500 samples are screened for presence of the one or more component of interest in less than an hour.

109. (New) The method of claim 105, wherein at least about 1000 samples are screened for the presence of the one or more component of interest in about 1 day.

110. (New) The method of claim 105, wherein the non-column-separated samples comprise cell lysate.

111. (New) The method of claim 105, wherein the non-column-separated samples comprise whole cells.

112. (New) The method of claim 105, wherein purifying the non-column-separated samples comprises attaching the enzyme library to a solid support.

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113. (New) The method of claim 112, wherein each enzyme in the library further comprises a tag moiety, and wherein the solid support comprises a tag binding moiety.

114. (New) The method of claim 113, wherein the tag moiety comprises biotin, avidin, or streptavidin and the tag binding moiety comprises biotin, avidin, or streptavidin.

115. (New) The method of claim 105, wherein the one or more component of interest comprises the enzyme substrate and the product of an enzymatic reaction, the method further comprising simultaneously quantifying the amount of the product of an enzyme reaction and the enzyme substrate.

116. (New) The method of claim 105, wherein performing flow injection analysis using electrospray tandem mass spectrometry comprises performing a method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry.

117. (New) The method of claim 116, comprising performing the neutral loss mass spectrometry or the parent ion mass spectrometry on a triple quadrupole mass spectrometer.

118. (New) The method of claim 117, wherein performing the neutral loss mass spectrometry comprises:

(a) scanning the one or more component of interest in a first quadrupole at a specified mass range;

(b) fragmenting the one or more component of interest in a second quadrupole by collision induced dissociation, thereby producing one or more neutral fragments and one or more daughter ion; and,

(c) detecting the one or more daughter ion.

119. (New) The method of claim 117, wherein performing the parent ion mass spectrometry comprises:

(a) scanning the one or more component of interest in a first quadrupole;

(b) fragmenting the one or more component of interest in a second quadrupole by collision induced dissociation; and,

(c) scanning a third quadrupole at a specified mass.

120. (New) The method of claim 105, wherein purifying comprises centrifugation.

121. (New) The method of claim 105, wherein purifying comprises filtration.

122. (New) The method of claim 105, wherein the off-line parallel purification system comprises an ion exchange resin.

123. (New) The method of claim 105, wherein the off-line parallel purification system comprises the addition of an organic solvent to the sample.

124. (New) The method of claim 105, wherein the off-line parallel purification system comprises a solid phase extraction plate.

125. (New) The method of claim 105, wherein an automatic sampler transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis at a rate of at least 100 samples an hour.

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126. (New) The method of claim 105, wherein 5 to 100 samples are pooled before performing flow-injection analysis using electrospray tandem mass spectrometry.